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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/966,724	10/01/2001	Kenneth W. Kinzler	01107.00193	3707

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EXAMINER	
ASHEN, JON BENJAMIN	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 12/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	Application No. 09/966,724	Applicant(s) KINZLER ET AL.	
	Examiner Jon B. Ashen	Art Unit 1635	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 22 November 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☒ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☐ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: _____.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☒ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☐ Other: _____.

ANDREW WANG
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Continuation of 11. does NOT place the application in condition for allowance because: Applicant's arguments are insufficient to overcome the outstanding rejections under 35 U.S.C. § 112 1st paragraph, written description and enablement. Applicants arguments have been fully considered but are not persuasive for the following reasons. Applicant's arguments with regard to Exhibits A-L were addressed in the Final Action mailed 8/24/05 (pgs. 3-7). Applicant has provided further argument that the state of the art of antisense, as shown by the James et al., was such that at least one antisense to any gene of a known coding sequence could be made, the full length one. However, this argument is not persuasive because disclosure of a single antisense that is full length and 100% complementary to a human MDM2 coding sequence is not a disclosure of a representative number of species from within the broad genus of antisense oligonucleotides, that are required to practice the claimed methods. Applicant's arguments with regard to Branch et al. (pgs. 6-7) are not persuasive because the disclosure of Branch et al., published 6 years after Applicant's filing date, indicates that in 1998, antisense in vitro to a gene where the coding sequence of the gene was known, was known in the art, but does not indicate that in 1992, at the time the instant invention was made, that antisense in vitro to any gene given the coding sequence of that gene, was described or known in the art. In regards to Applicant's arguments concerning the outstanding rejection under 35 U.S.C. § 112 1st paragraph, lack of enablement , Applicant's arguments have been fully considered but are not persuasive for the following reasons. Applicant's arguments with regards to Exhibits A-L (pg. 9) have been fully considered and are not persuasive for the reasons of record as set forth on pgs. 14-16 of the Action mailed 8/24/05. Applicant has further argued that Exhibits A-L teach antisense oligonucleotides for use in cells in vitro and that therefore, the instant in vitro methods, which are done in cells, are described. However, contrary to this position, Exhibits A-L do not disclose antisense to human MDM2. The abillty of the state of the art to administer antisense oligonucleotides to cells in vitro is not the basis of the outstanding rejection, but rather that it would have been required undue experimentation, based on the art recognized upredictability of antisense gene inhibition of a given gene, in cells in vitro at the time the instant invention was made given only the primary nucleotide coding sequence of that gene. Applicant has submittted Exhibits 1-4 and stated that they were not presented earlier because Applicant belived that the previoius response was sufficient. However, these Exhibits have not been considered because Applicant has not shown any good or sufficient reasons why the Exhibits are necessary and were not earlier presented. Morever, it is noted that Exhibits 1-4 appear to provide post-filiing disclosures that are significantly more detailed than the disclosure of the specifiction; i.e., that are not commensurate in scope with the instantly filed specification. Applicant has argued that the state of the art of antisense, with regard to the James et al. reference, was not unpredictable and that James et al. teaches that those of skill routinely made and used antisense oligonucleotides to successfully inhibit transcription or translation of a gene (pg. 13). However, contrary to Applicant's assertion, the James et al. reference, when viewed as a whole, sets forth that there is significant unpredictability in the art of antisense inhibition of gene expression in vitro at the time the instant invention was made (see pgs. 9-11, the Action mailed 8/24/05. Applicant has argued, in regards to the Branch et al. reference (pg. 14), that even if effective antisense molecules must be found empirically by screening, the claims are enabled if the experimentation required to identify those antisense molecules is merely routine, i.e., not undue. However, this argument is not persuasive because the amount of experimentation required to enable the instantly claimed methods in their full scope would indeed be undue, as set forth in the Action mailed 8/24/05 (pgs. 11-13). Applicant's arguments with regard to enablement in light of the Rojanaskul and Agrawal references were considered in the Action mailed 8/24/05. Applicant's arguments (pg. 15-16) concerning the "weight of the evidence" have been considered but are not persuasive. Contrary to Applicant's position and as set forth above and in the prior Actions, the Exhibits A-L do not provide sufficient evidence that, at the time the invention was made, the state of the art was in possession of antisense oligonucleotides to any gene given the primary nucleotide coding sequence of that gene or that the state of the art was enabled for what is now claimed, which is a method of inhibiting human MDM2 in cells in vitro, based soley on the recognition that antisense oligonucleotides could, generally, be used to inhibit gene transcription and translation. A showing that the state of the art recognized, generally, that antisense oligonucleotides to a gene could be made and used is not the specific guidance required by the skiled artisan, in light of the art recongnized unpredictability in the field of antisense, at the time th einvetion was made, to enable the instantly claimed methods that require the skilled artisan to make and use antisense oligonucleotides that will inhibit transcription or translation of a particular gene, the human MDM2 gene..